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Clinicopathological study of kidneys from patients on chronic dialysis

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Clinicopathological study of kidneys from patients on chronic dialysis. Kidneys removed from 58 pediatric patients at renal transplantation (except 3 cases), who had developed chronic renal failure and were maintained on dialysis, were investigated histopathologically, and the clinical profiles were taken into account. The patients ranged in age from 2 to 24 years, with an average of 11.2 years. The duration of dialysis ranged from 0.5 to 63 months, with an average of 12.6 months. The kidneys, which were conventionally prepared for histological observation, were subjectively divided into three groups depending on the degree of remaining nephrons. Patients with completely atrophic type (type 1), incompletely atrophic type (type 2), and mixed type of atrophy and hypertrophy (type 3) had a duration of dialysis of 20.0, 12.3, 6.3 months, respectively (Type 1 > Type 3, $P < 0.01$). A correlation between histology and function was demonstrated, since urinary output was more than 200 ml/day in most of the type 3 patients, and less than 20 ml/day in all of the patients with type 1. The findings suggest that the functioning nephrons that remained at the beginning of dialysis generally become atrophic within one year after the initiation of dialysis. The ratio of kidney weight to body weight showed a significant negative correlation with both the duration of dialysis and that of illness. The histopathological changes seen in kidneys of patients on dialysis were reviewed. The findings suggested that certain changes, unusual epithelial proliferations and oxalate deposition, are associated with persisting renal function rather than the duration of dialysis.

The possibility of long-term hemodialysis was envisioned in 1913 by Abel, and the foundations for the use of the artificial kidney in clinical medicine were laid by Kolff thirty odd years after. Since Scribner and his associates reported the first attempt of the treatment of chronic uremia by means of intermittent hemodialysis in 1960, dialytic therapy began to gain recognition in the treatment of chronic renal failure (CRF) [1]. With the remarkable development of this procedure, more than 80,000 patients are now maintained on dialysis in Japan, with several times that many world-wide.

While hemodialysis has made it possible for patients with CRF to remain alive for a long time, pathological studies associated with kidneys of such patients have been reported only sporadically, whereas "usual" end-stage kidneys have been well discussed [2–5]. Recently, acquired cystic kidney disease (ACKD) and renal neoplasms have been reported in kidneys of patients on long-term dialysis [6–17]. Although certain characteristic changes in such kidneys have been reported [18–32], many reports have not dealt with those kidneys from a general viewpoint. With few exceptions [20], little attention has been paid to the clinical aspects.

In this investigation, the pathology of end stage kidneys removed from 58 pediatric patients at renal transplantation (except 3 cases) who had developed CRF from various renal diseases and had been maintained on dialysis for varying periods was studied, as well as their relationships to the clinical data, including the duration of illness, the duration of dialysis, original disease, and urinary output. Although the periods of dialysis in the present study are rather short compared with those at which ACKD or renal neoplasms develop, it is necessary to pay attention to the pathological changes of kidneys which occur relatively early in dialysis.

Methods

Among 85 pediatric patients who developed CRF, were maintained on dialysis, and underwent nephrectomy at renal transplantation between 1974 and 1986 in Tokyo Metropolitan Children's Hospital, 58 were available for the present study. Five patients underwent unilateral nephrectomy and the rest bilateral nephrectomy after varying periods of dialysis. In three cases nephrectomy was performed at various intervals after transplantation. The patients, who ranged from 2 to 24 years of age (mean = 11.2), consisted of 29 males and 29 females.

The 111 removed kidneys were processed for microscopic examination by conventional techniques. One or two blocks were routinely dissected from each kidney so that they might reflect the whole lesion of the parenchyma. All slides from paraffin-embedded specimens were stained by hematoxylin and eosin (HE), and with periodic acid-Schiff (PAS) method when required.

The original diseases, diagnosed by needle biopsy or clinical examination, were divided into five categories (Table 1), depending on the similarities among the diseases, including the distribution of glomerular lesions (diffuse or focal) and the clinical picture. For example, in the (CGN + MPGN + RPGN) group, glomeruli are generally affected diffusely, so the histopathological picture at the end stage may be similar. The diagnostic term renal dysplasia/hypoplasia, or pyelonephritis/VUR, shows much the same clinical picture in each group.

First and foremost, the slides from all patients were examined microscopically. At least two slides (right and left) were examined for each patient (except for 3 patients with unilateral

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Table 1. Categorization of original diseases

Clinical diagnosis	CGN, MPGN, RPGN, CNS	HSPN, IgAN	FSGS	Dysplasia, hypoplasia	Pyeloneph. VUR	Others[a]
No. of cases	16	12	13	9	6	2
Age	11	13	11	13	11	3, 14
range: *years*	3–24	5–19	4–15	2–15	5–21	
Sex (M, F)	11, 5	6, 6	4, 9	4, 5	4, 2	0, 2
From onset to dialysis	41.7[b]	47.1	62.8	28.8	80.2	14.5
months	0-156	6–104	5-122	1-102	34-114	0, 29
Duration of dialysis	13.1	8.0	11.9	18.6	8.6	25.5
months	4-48	0.5–18	0.5-41	3-68	1.5–27	8, 43
Duration of illness	55.1	55.2	74.7	47.2	88.8	40.5
months	5–161	16–112	8-135	21–108	38–124	37, 44

Abbreviations are: CGN, chronic glomerulonephritis; RPGN, rapidly progressive glomerulonephritis; HSPN, Henoch-Schönlein purpura nephritis; FSGS, focal segmental glomerulosclerosis; MPGN, membranoproliferative glomerulonephritis; Pyeloneph., pyelonephritis; VUR, vesico-ureteral reflux; IgAN, IgA nephropathy; HUS, hemolytic uremic syndrome; CNS, congenital nephrotic syndrome.

[a] Include HUS and Takayasu's disease

[b] The onset time was unclear in one case of CGN.

nephrectomy), without any information about the clinical profile. Depending on the degree of remaining nephrons, which consist of nearly intact glomeruli and convoluted tubules around them, the kidneys were divided subjectively into the three groups described below. All slides were also examined under polarized light to explore oxalate deposit.

The relationships among duration of dialysis, duration of illness, original disorder, urinary output, ratio of kidney weight to body weight, and the classification were evaluated.

Furthermore, histopathological changes frequently recognized in end stage kidneys from the patients on dialysis were reviewed and certain changes were analyzed in association with the classification described herein.

Results

Classification of kidneys from patients on dialysis

Type 1: Completely atrophic type (Fig. 1A). In this type, the renal parenchyma is almost uniformly deteriorated. Glomeruli are solidified or obsolescent and tubules have disappeared or exhibit marked atrophy of a much smaller caliber than normal.

Type 2: Incompletely atrophic type (Fig. 1B). In this type, most of the renal parenchyma is atrophic. There are, however, scattered "still-functioning" nephrons which consist of unaffected or slightly affected glomeruli and almost normal convoluted tubules adjacent to them. However, they exhibit none or only a few of the hypertrophic changes common in the following type.

Type 3: Mixed type of atrophy and hypertrophy (Fig. 1C). In this type, there are hypertrophic changes in the proximal convoluted tubules other than atrophy. The tubules show enlargement of the lumen and epithelium. Epithelial proliferation is sometimes found in the form of papillary projections into the lumen.

Each of these three types may reflect the degree or distribution of renal lesions just at the initiation of dialysis on the one hand, and be affected by further progress of the original disorder, compensatory hyperperfusion, ischemia caused by arterial narrowing common in end stage kidneys, supervening infection, and disuse on the other.

Relationship between the classification of types 1 to 3 and duration of dialysis

According to the criteria described above, the 58 cases were divided into three groups. Twenty cases were classified as type 1, and the duration of dialysis ranged from 2.5 to 68 months, with an average of 20.0 months (Fig. 2A). Fifteen cases were of type 2, with a history of dialysis ranging from 2 to 43 months, averaging 12.3 months. There were 23 cases with type 3. The patients had been treated by dialysis for 0.5 to 27 months with an average of 6.3 months. The duration of type 1 was significantly longer than that of type 3 ($P < 0.01$), but there were no other significant differences in duration of dialysis among the three groups ($P > 0.05$).

Among the 23 patients with type 3, 21 had a history of dialysis of 12 months or less, and among the type 1 cases, 15 of the 20 had been maintained on dialysis longer than 9 months. These findings suggest that nephrons that were hypertrophied at the beginning of dialysis become atrophic around one year after the initiation of dialysis.

The duration of illness from onset to nephrectomy ranged from 5 to 161 months. No significant correlation was found between the duration of illness and that of dialysis ($P > 0.05$). Therefore, the two periods could be regarded as independent of each other. There were no significant differences in duration of illness among the three groups ($P > 0.05$).

For each group according to the original disease, a tendency was shown for the kidneys of the patients with a longer history of dialysis to be type 1, and for those with shorter-term dialysis to be type 3 (Fig. 2B).

Relationship between classification and urinary output

In 51 of the 58 cases, the volume of urinary output at nephrectomy was recorded. In type 1 (18 cases), the patients showed very little urinary output (less than 20 ml/day). Most patients with type 3 (19 of 21 cases) had urinary output of more than 200 ml/day. In type 2 (12 cases), both types were present (4 with urinary output of more than 100 ml/day and 8 with less). The urine was not analyzed qualitatively.

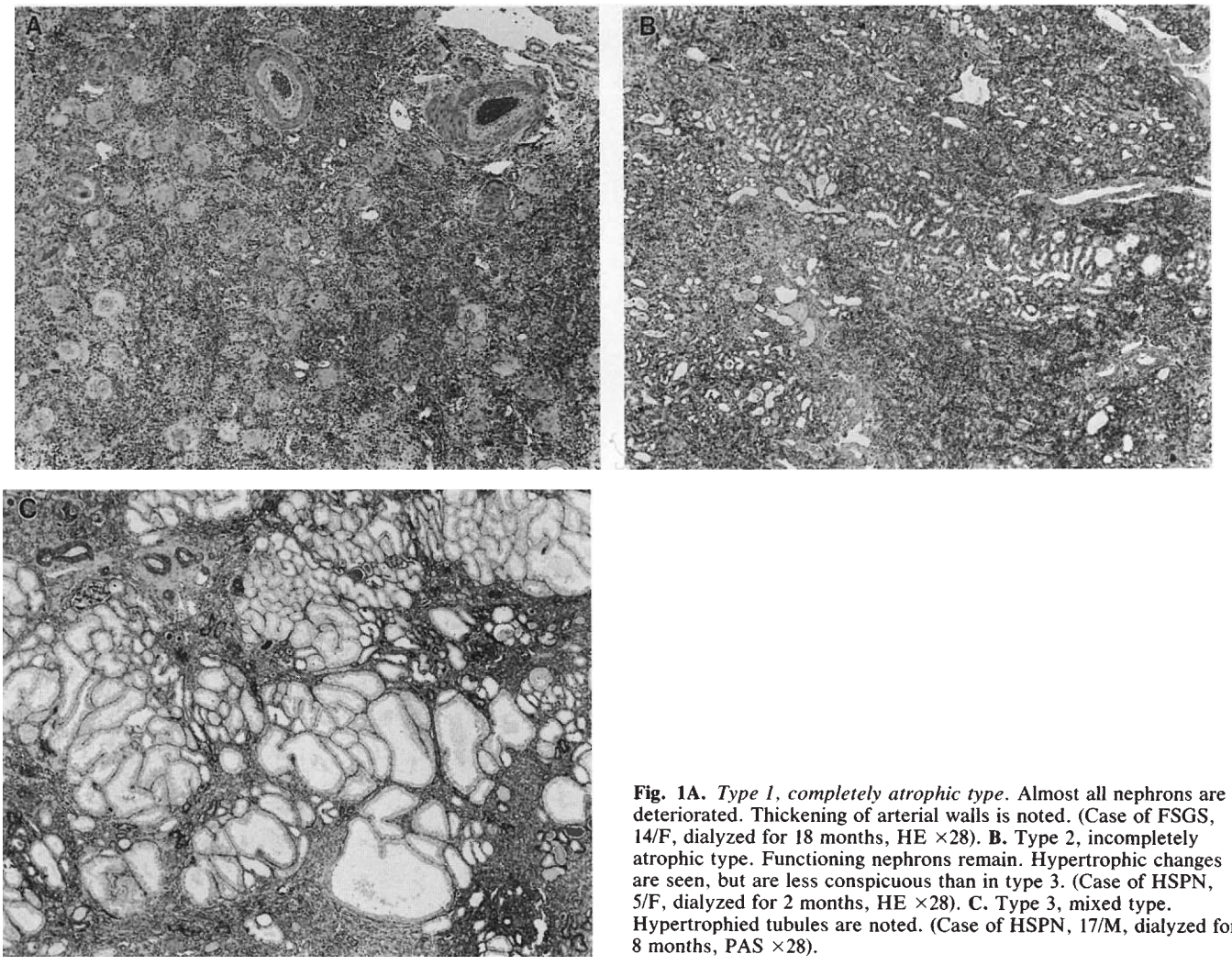

Fig. 1A. *Type 1, completely atrophic type.* Almost all nephrons are deteriorated. Thickening of arterial walls is noted. (Case of FSGS, 14/F, dialyzed for 18 months, HE ×28). **B.** Type 2, incompletely atrophic type. Functioning nephrons remain. Hypertrophic changes are seen, but are less conspicuous than in type 3. (Case of HSPN, 5/F, dialyzed for 2 months, HE ×28). **C.** Type 3, mixed type. Hypertrophied tubules are noted. (Case of HSPN, 17/M, dialyzed for 8 months, PAS ×28).

Relationship between duration of dialysis and ratio of kidney weight to body weight

For 103 of the 111 kidneys removed from the 58 patients, the weight had been recorded (Fig. 3). Seventeen kidneys from nine patients with renal dysplasia or hypoplasia were excluded. Among the remaining 86 kidneys, the relationship between the period of dialysis and the ratio of kidney weight to body weight was determined. The mean ratio was 0.18%, and a negative correlation was demonstrated ($r = -0.42$, $N = 86$, $P < 0.01$). At the same time, the ratio correlated negatively with the duration of illness ($r = -0.50$, $N = 84$, $P < 0.01$, data not shown).

Histopathological changes in kidneys from patients on dialysis

Embryonal hyperplasia of Bowman's capsular epithelium (EHBCE) is characterized by clusters of embryonal, undifferentiated cells in association with obsolescent or sclerosed glomeruli (Fig. 4A). The clusters show a tubular or papillary structure composed of small undifferentiated cells consisting of an oval or round hyperchromatic nucleus and inconspicuous cytoplasm with a delicate basement membrane beneath them. As shown by Hughson, McManus and Hennigar [24], EHBCE is distinct from pseudotubules (described below) and adenomatoid or metaplastic lesions of the glomerular capsular epithelium found in nonrenal neoplastic disorders [33–35]. EHBCE was found in 18 of the 58 cases (31%). The incidence among patients with type 3 (8.7%) was lower than that in the other two groups (type 1: 40%; type 2: 53%, $P < 0.01$). There was no difference in the duration of dialysis between the groups with and without EHBCE ($P > 0.05$).

Interstitial epithelial proliferation (IEP) is characterized by small epithelium which proliferates in the interstitium of the renal cortex or medulla, forming a tubular structure surrounded by a basement membrane (Fig. 4B). The epithelial cell consists of a small hyperchromatic round or oval nucleus and inconspicuous cytoplasm. IEP was found in 35 of the 58 cases (60%). As with EHBCE, the incidence of IEP in type 3 (35%) was lower than in the other two groups (type 1: 70%; type 2: 80%; type 3 < type 1; $P < 0.05$; type 3 < type 2; $P < 0.01$). There were no differences in the duration of dialysis between the groups with and without IEP ($P > 0.05$).

In addition to conventional cysts that may have been due to

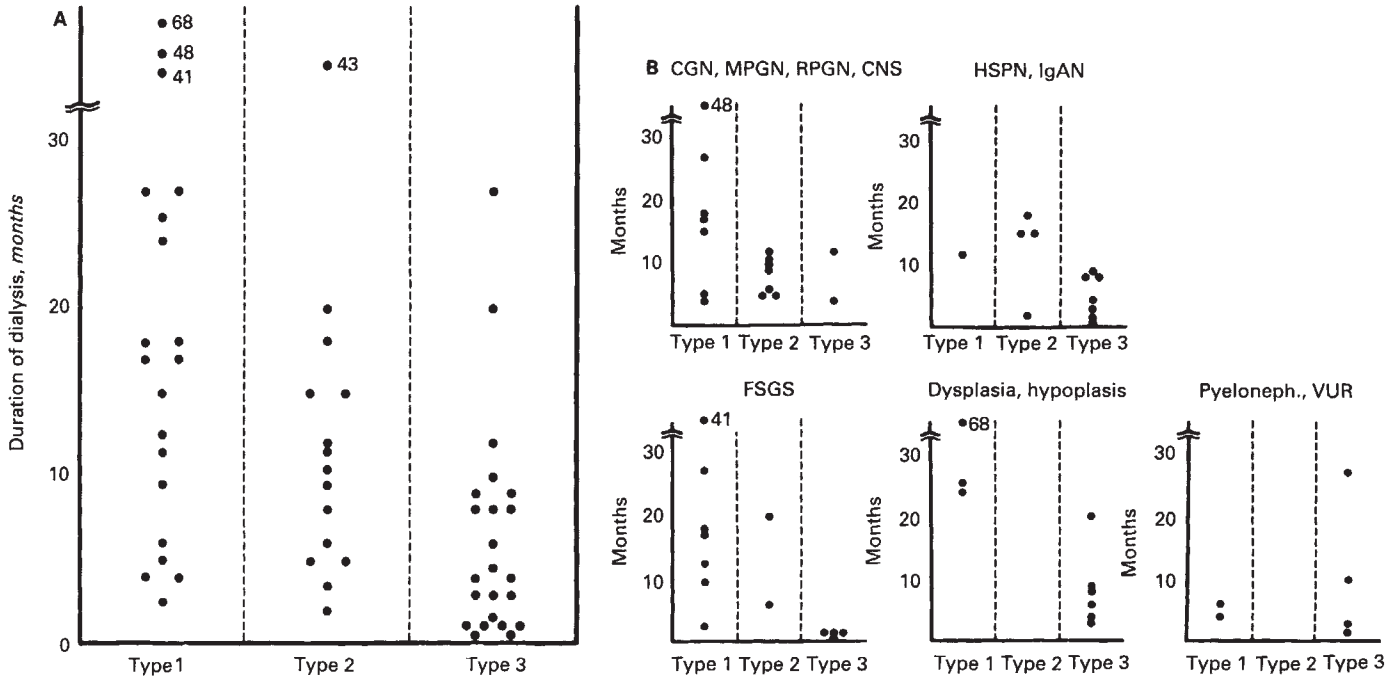

Fig. 2A. *Relationships between the three groups and duration of dialysis (In type 1 > in type 3, $P < 0.01$).* **B.** Relationships between three groups and duration of dialysis in each category of original disease.

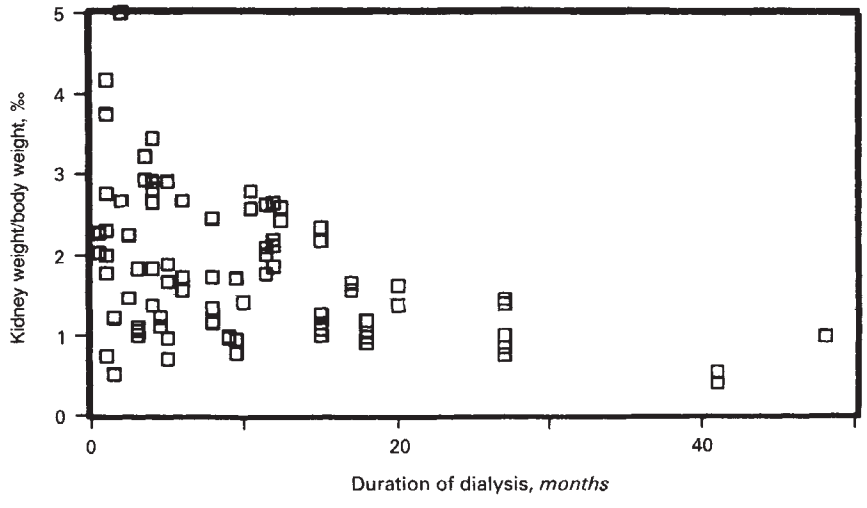

Fig. 3. *Relationship between the ratio of kidney weight to body weight and duration of dialysis.*

tubular dilatation [12], atypical cysts originating in the glomeruli were frequently seen. Their walls consisted of fibrous tissue containing a basement membrane and a layer of flattened epithelium (Fig. 4C). Because of the transitional form between cystic dilatation of Bowman's space and a complete cyst devoid of a tuft, a glomerular origin is suggested. Glomerular cysts were found in 27 of the 58 cases (47%). There were no significant differences in their occurrence among the three groups (type 1: 50%; type 2: 33%; type 3: 52%, $P > 0.05$), or between the duration of dialysis in the groups that did or did not have glomerular cysts ($P > 0.05$).

Oxalate crystals were deposited most frequently in the tubules, and sometimes in tubular epithelium or the interstitium. They are identified as light yellow-brown crystals in HE-stained sections, and are birefringent under polarized light (Fig. 4D). They were accompanied not infrequently by a foreign body reaction. Deposition of oxalate crystals was demonstrated in 32 of the 58 cases (55%) when all slides were examined under polarized light. The incidence in type 3 (35%) was lower than in the other two groups (type 1: 70%; type 2: 67%, $P < 0.05$). The severity of oxalate deposition was not investigated in the present study. There was no difference in the duration of dialysis between the groups with and without oxalate deposition ($P > 0.05$).

Adenomatous hyperplasia of tubular epithelium is usually associated with cortical hypertrophic tubules. It is character-

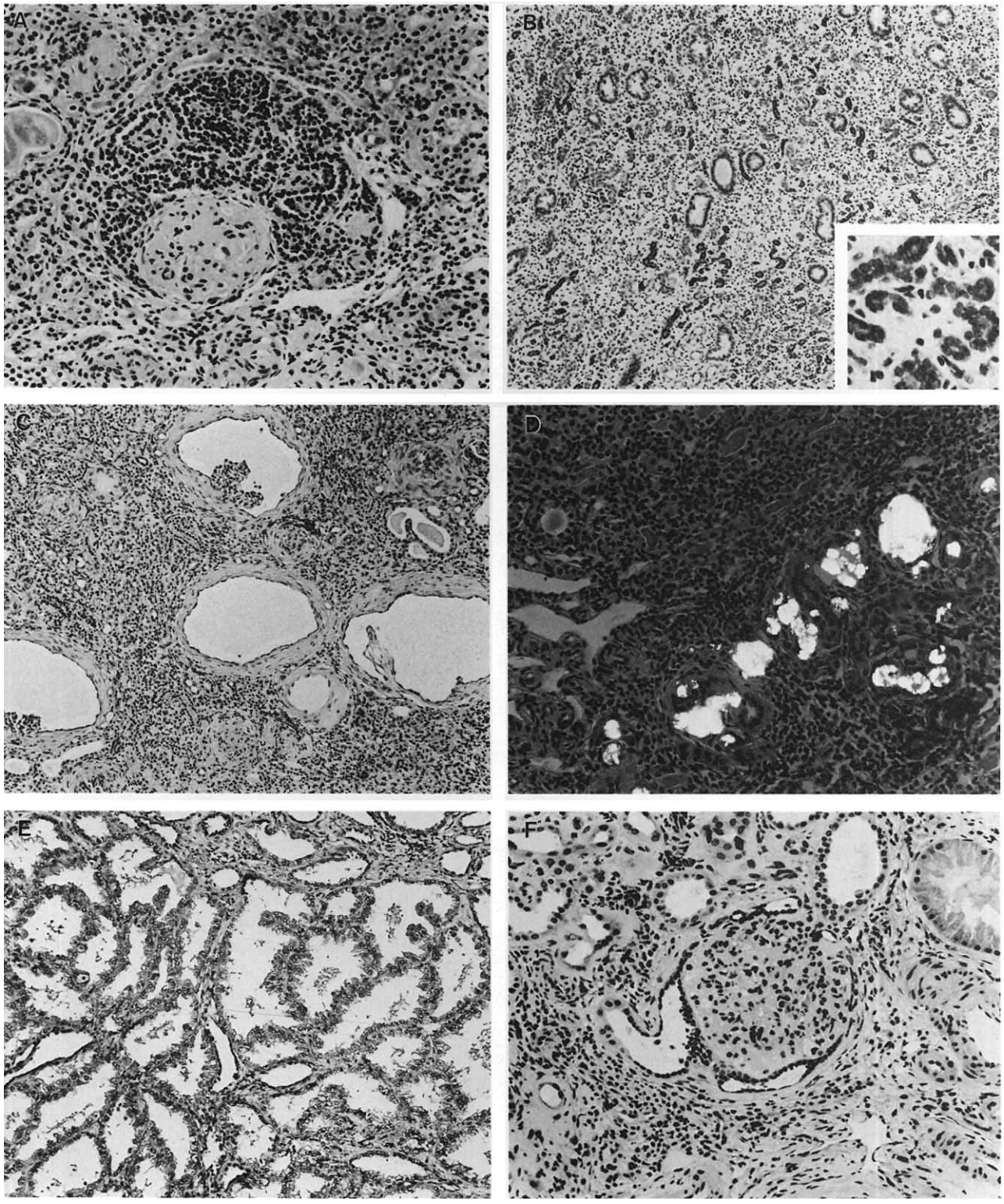

Fig. 4A. *Embryonal hyperplasia of Bowman's capsular epithelium.* (Case of FSGS, 12/F, dialyzed for 27 months, Type 1, HE ×140). **B.** Interstitial epithelial proliferation. (Case of HSPN, 9/M, dialyzed for 15 months, Type 2, HE ×70, inset ×280). **C.** A glomerular cyst. (Case of RPGN, 7/M, dialyzed for 4 months, Type 1, HE ×70). **D.** Oxalate deposition in tubules. (Case of pyelonephritis, 11/M, dialyzed for 10 months, Type 3, HE ×70, viewed with polarized light). **E.** Adenomatous hyperplasia in proximal convoluted tubules. (Case of dysplasia, 15/F, dialyzed for 6 months, Type 3, HE ×70). **F.** Obsolescent glomerulus with pseudotubule. (Case of HSPN, 9/M, dialyzed for 15 months, Type 2, HE ×140).

ized by epithelial enlargement, proliferation, and sometimes papillary projections into an enlarged lumen (Fig. 4E). Slight cellular atypism was sometimes seen.

Arteries and arterioles showed marked narrowing with intimal thickening and medial hypertrophy.

Glomeruli showed global sclerosis or original lesions such as lobulation, crescent formation, and segmental hyalinosis. Fibrous thickening of the parietal wall of Bowman's capsule, inflammatory cell infiltration around solidified glomeruli, and sometimes a layer of cells covering a solidified tuft or Bowman's parietal wall were found. This layer of cells, possibly originating in the epithelium, formed pseudotubules around solidified or obsolescent glomeruli (Fig. 4F) [5], a condition which is morphologically distinct from EHBCE (described above).

Tubules disappeared or showed marked atrophy to a much smaller caliber, or occasionally microcystic dilatation with a flattened epithelium. Thickening of the tubular basement membrane and casts of polymorphonuclear leukocytes were sometimes found.

The interstitium was fibrous with various mixtures of chronic inflammatory cells. Lymphoid follicles with germinal centers were sometimes seen.

Discussion

The classification of kidneys from the patients on dialysis into three groups, depending on the degree of remaining nephrons, seems to be an advantage in analyzing them systematically and to be interesting for clinicians because they could speculate on the status of patients' kidneys on the basis of their clinical history. In the present study, it was demonstrated that the degree of remaining nephrons generally correlates with the renal function. From the morphological and functional points of view, functioning nephrons generally seem to become atrophic in one year or less after the initiation of dialysis. It was suggested that as far as atrophy of functioning nephrons is concerned, the factor of disuse plays an important role, because kidneys of type 3 had a history not of shorter duration of illness, but of shorter history of dialysis, which would represent the period of replacement of renal function by the artificial kidney.

Ishikawa et al showed in their study of 130 adult cases by computed tomography that kidney volume decreased progressively up to three years after the initiation of dialysis, and thereafter increased in a number of cases because of cyst formation [10]. In the present study, the ratio of kidney weight to body weight was used as an indicator of renal size because the patients' ages were so wide-ranging that it was impossible to evaluate the size of the kidney uniformly only on the basis of kidney weight. The ratio correlated negatively with both the duration of dialysis and that of illness. However, no tendency for the ratio to increase was demonstrated, possibly because ACKD had not developed in the patients in the present study.

Histological studies have revealed vascular changes [18–23, 30], oxalate deposits [30–32, 36], EHBCE [24], cyst formation including acquired polycystic disease [6–9, 11–13, 15–17, 25], and others [26, 27, 29]. According to the morphometric studies on arterial changes previously described [20, 22] but not performed in the present study, the degree of intimal thickening is correlated with the duration of dialysis. Some possible explanations have been suggested. Accelerated arteriosclerosis [18, 19], the existence of high blood pressure, metabolic or hemodynamic changes brought about by dialysis [20], and disuse endarteritis [22] or disuse atrophy [3] have been suggested. Zobl et al related intimal fibrosis to decreased perfusion of the kidneys during hemodialysis [20]. It is interesting that the increase in polyamines in uremic serum might be atherogenic [37]. Nodule formation in intrarenal arteries and arterioles [23] was not seen in the present series.

Although adenomatous hyperplasia of the tubular epithelium is not frequently found in autopsy cases of CRF not supported by dialysis, it seems to turn to atrophy, and could be regarded as a hypertrophic reaction due to compensatory hyperfiltration [38–40]. So the possibility of malignant transformation would be deniable.

EHBCE was first described by Hughson et al [24], and unusual epithelial proliferation associated with dialysis was previously reported by McManus et al, who described epithelial proliferation forming a tubular structure in association with vessels or nerves [26, 27]. EHBCE and IEP seem to be rather specific for kidneys of dialyzed patients because these changes are not usually observed in autopsy cases associated with CRF not maintained on dialysis. The fact that the occurrences of EHBCE and IEP were significantly lower in type 3 than in the other two types suggests that they may have a similar background for their genesis. This dialysis-related epithelial proliferation may be associated with the degree of remaining renal function, excretion of urine, rather than with the duration of dialysis. Of course, the latter can influence the former. It is possible that polyamines retained in uremic serum and not removed by dialysis play an important role in this unusual cell proliferation [37]. However, one patient with urinary output of more than 400 ml/day had EHBCE and IEP, so other factors may be involved in its genesis.

Cysts with atypical or neoplastic epithelium were previously described in association with ACKD [6–11, 13, 15–17, 25]. According to these reports, atypical cysts are lined with multilayered columnar epithelium, sometimes with papillary projections into the cystic space. In the present study, atypical cysts of that kind were not generally seen but cysts originating in glomeruli were frequently seen. Glomerular cysts, previously reported in association with cystic disease [41–44], have been found in patients undergoing dialysis [12, 44]. The mechanism by which glomerular cysts arise could be explained as the enlargement of Bowman's capsular space with atrophy or disappearance of tufts because of tubular occlusion adjacent to glomeruli accompanied by fibrous thickening of Bowman's parietal walls. Cysts due to tubular dilatation were also found, but not to the extent found in acquired polycystic kidney.

As concerns oxalate crystal deposits, a correlation between the extent of deposition and the duration of renal failure [31] or dialysis [30, 32] has been reported. Oxalate is excreted only by the kidneys, and the finding that the kidneys of type 3 exhibited oxalate deposition at a significantly lower frequency than those of the other two types suggests that it is associated with the degree of remaining functioning nephrons. In addition, metabolic disorders of oxalate and individual variations should be taken into account.

Neoplastic lesions like renal cell carcinoma were not found in this study, unless EHBCE or IEP is regarded as a neoplasm. This may be due to the use of pediatric cases, and to the rather

short periods of dialysis in the present study in comparison with other descriptions of neoplasms developing in kidneys on long-term dialysis [6–11, 13–17]. Although EHBCE or IEP was found rather frequently in the present study, about 30 and 60%, respectively, reports of these lesions are rare [24, 27]; we have not had any autopsied cases in our laboratory where the proliferative lesion of poorly differentiated epithelium was found in end-stage atrophic kidneys from adult patients on dialysis. Therefore, such unusual epithelial proliferations as EHBCE or IEP might be rather restricted to kidneys of younger patients on dialysis. Leichter et al investigated pediatric patients on dialysis by magnetic resonance imaging and ultrasonography [17]. They reported that 15 of 42 patients maintained on dialysis for more than two years developed ACKD and one of them developed neoplastic tubular changes, which were scattered throughout the renal parenchyma and consisted of small cells with hyperchromatic nuclei forming tubules with micropapillae extending into the lumina. It is not clear whether this neoplastic change is the same as the proliferation of poorly differentiated epithelium seen in the present study.

Although a detailed comparative investigation was not conducted in the present study, the histopathological differences between kidneys after dialysis and without dialysis would be the occurrence of unusual epithelial proliferations and the very frequent occurrence of glomerular cysts. Perhaps oxalate deposition would occur more frequently in the former, for the possibility cannot be excluded that these changes were caused not by dialysis but by the state of prolonged uremia in which patients could not be alive without dialysis.

In conclusion, end stage kidneys from 58 pediatric patients who had developed CRF and were sustained by dialysis for varying periods were histopathologically reviewed and analyzed in association with clinical data. In the facts that pediatric cases were evaluated, that the duration of dialysis was generally rather short, and that the relationships between pathological and clinical findings were discussed, the present study differs from previous ones. Further study is required to evaluate end-stage kidney disease in which acquired polycystic kidney disease or neoplasms may develop during long-term dialysis.

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References

1. BLUEMLE LW JR: Current status of chronic hemodialysis. *Am J Med* 44:749–766, 1968
2. HEPTINSTALL RH: Pathology of end-stage kidney disease. *Am J Med* 44:656–663, 1968
3. KINCAID-SMITH P: *The Kidney: A Clinico-pathological Study*. Oxford, Blackwell, 1975, pp. 393–399
4. VELOSA J, MILLER K, MICHAEL AF: Immunopathology of the end-stage kidney. *Am J Pathol* 84:149–162, 1976
5. HEPTINSTALL RH: *Pathology of the Kidney* (3rd ed). Boston, Little Brown, 1983, Vol 2, pp. 601–636
6. DUNNILL MS, MILLARD PR, OLIVER D: Acquired cystic disease of the kidneys: A hazard of long-term intermittent maintenance haemodialysis. *J Clin Pathol* 30:868–877, 1977
7. KONISHI F, MUKAWA A, KITADA H: Acquired cystic disease of the kidney and renal cell carcinoma on long term hemodialysis—Four surgical cases of young adults in Japan. *Acta Pathol Jpn* 30: 847–858, 1980
8. KREMPIEN B, RITZ E: Acquired cystic transformation of the kidneys of haemodialysed patients. *Virchows Arch* 386:189–200, 1980
9. FAYEMI AO, ALI M: Acquired renal cysts and tumors superimposed on chronic primary kidney disease: An autopsy study of 24 patients. *Pathol Res Pract* 168:73–83, 1980
10. ISHIKAWA I, SAITO Y, ONOUCHI Z, KITADA H, SUZUKI S, KURIHARA S, YURI T, SHINODA A: Development of acquired cystic disease and adenocarcinoma of the kidney in glomerulonephritic chronic hemodialysis patients. *Clin Nephrol* 14:1–6, 1980
11. HUGHSON MD, HENNIGAR GR, MCMANUS JFA: Atypical cysts, acquired renal cystic disease, and renal cell tumors in end stage dialysis kidneys. *Lab Invest* 42:475–480, 1980
12. FEINER HD, KATZ LA, GALLO GR: Acquired cystic disease of kidney in chronic dialysis patients. *Urology* 17:260–264, 1981
13. CHUNG-PARK M, RICANATI E, LANKERANI M, KEDIA K: Acquired renal cysts and multiple renal cell and urothelial tumors. *Am J Clin Pathol* 79:238–242, 1983
14. ISHIKAWA I, ONOUCHI Z, SAITO Y, TATEISHI K, SHINODA A, SUZUKI S, KITADA H, SUGISHITA N, FUKUDA Y: Sex differences in acquired cystic disease of the kidney on long-term dialysis. *Nephron* 39:336–340, 1985
15. GEHRIG JJ JR, GOTTHEINER TI, SWENSON RS: Acquired cystic disease of the end-stage kidney. *Am J Med* 79:609–620, 1985
16. HUGHSON MD, BUCHWALD D, FOX M: Renal neoplasia and acquired cystic kidney disease in patients receiving long-term dialysis. *Arch Pathol Lab Med* 110:592–601, 1986
17. LEICHTER HE, DIETRICH R, SALUSKY IB, FOLEY J, COHEN AH, KANGARLOO H, FINE RN: Acquired cystic kidney disease in children undergoing long-term dialysis. *Pediatr Nephrol* 2:8–11, 1988
18. LINDNER A, CHARRA B, SHERRARD DJ, SCRIBNER BH: Accelerated atherosclerosis in prolonged maintenance hemodialysis. *N Engl J Med* 290:697–701, 1974
19. LUNDIN AP, FRIEDMAN EA: Vascular consequences of maintenance hemodialysis—An unproven case. *Nephron* 21:177–180, 1978
20. ZOBL H, SCHIEBELER A, RIES P, BAHLMANN J: Die obliterative Intimafibrose der Nierenarterien unter Einfluß der Hämodialyse bei Patienten mit chronischer Niereninsuffizienz. *Virchows Arch* 369: 131–141, 1975
21. TRILLO A: Ultrastructure of proteoglycans in human renal arteries from end stage renal disease. *Atherosclerosis* 28:161–169, 1977
22. NISHI T, BOND C JR, BROWN G, SOLEZ K, HEPTINSTALL RH: A morphometric study of arterial intima thickening in kidneys of dialyzed patients. *Am J Pathol* 95:597–610, 1979
23. MCMANUS JFA, HUGHSON MD, FITTS CT, WILLIAMS AV: Studies on "end-stage" kidneys. 1. Nodule formation in intrarenal arteries and arterioles. *Lab Invest* 37:339–349, 1977
24. HUGHSON MD, MCMANUS JFA, HENNIGAR GR: Studies on "end-stage" kidneys. 2. Embryonal hyperplasia of Bowman's capsular epithelium. *Am J Pathol* 91:71–84, 1978
25. MCMANUS JFA, HUGHSON MD: Focal atypical hyperplasia of tubule epithelium with cyst formation in end-stage/dialysis kidney. (abstract) *Fed Proc* 37:670, 1978
26. MCMANUS JFA, HUGHSON MD: Studies on end-stage kidneys. 5. Unusual epithelial activity or remarkable endothelial metaplasia. Findings in a dialyzed kidney. *Am J Surg Pathol* 3:229–234, 1979
27. MCMANUS JFA, HUGHSON MD, HENNIGAR GR, FITTS CT, RAJAGOPALAN PR, WILLIAMS AV: Dialysis enhances renal epithelial proliferations. *Arch Pathol Lab Med* 104:192–195, 1980
28. MCMANUS JFA, HUGHSON MD: New therapies and new pathologies. End-stage-dialysis kidneys. *Arch Pathol Lab Med* 103:53–57, 1979
29. HUGHSON MD, MCMANUS JFA, FITTS CT, WILLIAMS AV: Studies of end-stage kidneys. 3. Glycogen deposition in interstitial cells of the renal medulla. *Am J Clin Pathol* 72:400–404, 1979

30. FAYEMI AO, ALI M: The pathology of end-stage renal disease in hemodialysis patients. *Israel J Med Sci* 15:901–909, 1979
31. SALYER WR, KEREN D: Oxalosis as a complication of chronic renal failure. *Kidney Int* 4:61–66, 1973
32. FAYEMI AO, ALI M, BRAUN EV: Oxalosis in hemodialysis patients. A pathologic study of 80 cases. *Arch Pathol Lab Med* 103:58–62, 1979
33. EISEN HN: Adenomatoid transformation of the glomerular capsular epithelium. *Am J Pathol* 22:597–601, 1946
34. EULDERINK F: Adenomatoid changes in Bowman's capsule in primary carcinoma of the liver. *J Pathol Bact* 87:251–254, 1964
35. REIDBORD HE: Metaplasia of the parietal layer of Bowman's capsule. *Am J Clin Pathol* 50:240–242, 1968
36. CHAPLIN AJ: Histopathological occurrence and characterisation of calcium oxalate: A review. *J Clin Pathol* 30:800–811, 1977
37. BAGDADE JD, SUBBAIAH PV, BARTOS D, BARTOS F, CAMPBELL RA: Polyamines: An unrecognised cardiovascular risk factor in chronic dialysis? *Lancet* 1:412–413, 1979
38. MALT RA: Compensatory growth of the kidney. *N Engl J Med* 280:1446–1459, 1969
39. PREUSS HG: Compensatory renal growth symposium: An introduction. *Kidney Int* 23:571–574, 1983
40. KENNER CH, EVAN AP, BLOMGREN P, ARONOFF GR, LUFT FC: Effect of protein intake on renal function and structure in partially nephrectomized rats. *Kidney Int* 27:739–750, 1985
41. VLACHOS J, TSAKRAKLIDIS V: Glomerular cysts. An unusual variety of "polycystic kidneys": Report of two cases. *Am J Dis Child* 114:379–384, 1967
42. TAXY JB, FILMER RB: Glomerulocystic kidney. Report of a case. *Arch Pathol Lab Med* 100:186–188, 1976
43. KROUS HF, RICHIE JP, SELLERS B: Glomerulocystic kidney. A hypothesis of origin and pathogenesis. *Arch Pathol Lab Med* 101:462–463, 1977
44. MCALISTER WH, SIEGEL MJ, SHACKELFORD G, ASKIN F, KISSANE JM: Glomerulocystic kidney. *Am J Roentgenol* 133:536–538